

- (c) at least one amino acid;
- (d) a surfactant; and
- (e) an inorganic acid as a buffering agent,

wherein the lyophilizate is essentially free of polyethylene glycols and additional proteins.

REMARKS

The Office Action of December 18, 2001 has been reviewed and the foregoing amended claims and the comments set forth below are a complete response thereto.

Claims 13 and 15-36 are all the pending claims. In the Office Action, there is a typographical error indicating that claim 115 is rejected. Applicants submit that there is no claim 115, and request that the examiner correct the record on this point.

By this Amendment, claim 27 has been amended to recite that the lyophilizate is essentially free of polyethylene glycols and additional proteins. No new matter has been added, and entry of the amended claim is requested.

I. Response to Rejection of Claims 13, 15-26 and 36 under 35 U.S.C. §112, second paragraph

Claims 13, 15-26 and 36 are rejected under 35 U.S.C. §112, second paragraph, for reciting the phrase "essentially free", which according to the Examiner, is indefinite.

As noted by the Examiner, in order for the claims to recite "essentially free", the specification must contain guidelines and examples sufficient to enable a person of ordinary skill in the art to understand that "essentially" was used to account for sources with only polyethylene glycol and additional protein impurities in them.

Applicants traverse for the following reasons.

On page 5 at line 30 continued to page 6, line 10, the specification teaches the disadvantages of compositions containing polyethylene glycol and additional protein impurities, and that to avoid toxicity or adverse immunological reactions for any such composition of the invention, the composition must be "essentially free" of these components.

Notably, the Examiner's cited reference, Michaelis, does not even define the meaning of "essentially free" with respect to polymeric auxiliary substances (see below discussion). Applicants submit that the meaning of the phrase would be relative to the field of art with respect to polymer concentration ranges in lyophilizates, and that its meaning would be well understood to one of skill in this art field. Accordingly, withdrawal of the rejection is deemed proper.

II. Response to Rejection of Claims 13, 15-21 and 23-36 under 35 U.S.C. §102(e)

Claims 13, 15-21, and 23-36 are rejected under 35 U.S.C. §102(e) as being anticipated by Andya (USPN 6,267,958).

According to the Examiner, the claims are *prima facie* anticipated by Andya which broadly teaches lyophilizates and methods for producing lyophilizates upon which the instant claimed invention reads.

Applicants traverse for the following reasons.

In order for Andya to be an effective reference under §102(e), it must disclose each and every element of the claimed invention, it must have been filed prior to an applicants' date of invention, **and** it must be "by another". Andya does not teach or suggest all of the claimed elements, therefore, the reference is not effective under §102(e).

Even though Andya discloses a water-soluble lyophilizate comprising a monoclonal or polyclonal antibody, a sugar or amino sugar, at least one amino acid, and a surfactant, wherein the lyophilizate is essentially free of contaminating proteins (less than 5%; Col. 7, lines 17-25), significantly, Andya specifically **includes** polyethylene glycols as a "lyoprotectant" in its formulation (Col. 9, line 30). In this respect, Andya teaches away from the instant claimed lyophilizate which specifically excludes the presence of polyethylene glycols. Andya is not an effective reference with respect to any of the pending generic claims 13 and 36. Withdrawal of the rejection is deemed proper.

III. Response to Rejection of Claims 13 and 15-36 under 35 U.S.C. §103(a)

Claims 13 and 15-36 are rejected under 35 U.S.C. §103(a) as being obvious over Andya in view of Michaelis (USPN 5,919,443).

The Examiner considers the instant claims *prima facie* obvious over the Andya and Michaelis, since Andya allegedly teaches the claimed invention for the reasons set forth under the anticipation rejection and Michaelis teaches the amino sugars of claim 22.

Applicants traverse for the following reasons.

Michaelis specifically teaches the disadvantages of including high-molecular weight polymers (Col. 2, lines 15-29; Col. 3, lines 29-32) in its preparation. Significantly, Michaelis teaches that the preparations are "essentially free of ...polymeric auxiliary substances". This teaching is in distinct contrast to Andya, the preparation of which **necessarily** contains polymeric auxiliary substances to achieve the object of Andya's invention, namely, improved stabilization of the protein. Accordingly, where Andya teaches away from Michaelis, one skilled in the art would not have found any motivation to combine the references.

Michaelis is specifically silent with respect to the lyophilizate being formulated to contain a protein other than G-CSF. Michaelis does not make general disclosures for the

use of the formulation in stabilizing any other protein, accordingly, one skilled in the art would not have been motivated to modify Michaelis to obtain the instant lyophilizate for an antibody.

Michaelis does not define the meaning of "essentially free" with respect to polymeric auxiliary substances. Applicants submit that the meaning of the phrase would be relative to the field of art with respect to polymer concentration ranges in lyophilizates, and that its meaning would be well understood to one of skill in this art field.

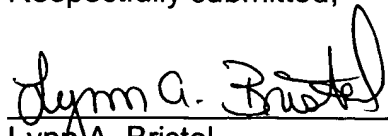
Accordingly, in view of the foregoing comments, Applicants submit that the claims are nonobvious and that withdrawal of the rejection is deemed proper.

CONCLUSION

In view of the amended claim and all of the foregoing arguments, Applicants submit that the Examiner's rejection of the claims under 35 U.S.C. §§102(e), 103(a) and 112, second paragraph, have been met and overcome. Applicants request that the Examiner allow the application to pass to issuance.

The Commissioner is hereby authorized to charge any fee deficiency or credit any overpayment associated with this communication to Deposit Account No. 01-2300.

Respectfully submitted,


Lynn A. Bristol
Registration No. 48,898

Customer No. 004372
ARENT FOX KINTNER PLOTKIN & KAHN, PLLC
1050 Connecticut Avenue, N.W., Suite 400
Washington, D.C. 20036-5339
Tel: (202) 857-6000; Fax: (202) 638-4810

LAB/ejb

MARKED-UP COPY OF THE CLAIMS FOR 09/308,223

27. (Amended) A lyophilizate, consisting essentially of

[(1)] (a) a monoclonal antibody or a polyclonal antibody;

[(2)] (b) a sugar or an amino sugar;

[(3)] (c) at least one amino acid;

[(4)] (d) a surfactant; and

[(5)] (e) an inorganic acid as a buffering agent,

wherein the lyophilizate is essentially free of polyethylene glycols and additional proteins.